Summary of Safety and Effectiveness Data

A. General Information

Device Generic Name: Transcatheter Patent Ductus Arteriosus Occlusion Device

Device Trade Name: AMPLATZER® Duct Occluder
AMPLATZER® 180° Delivery System
AMPLATZER® 180° Exchange System

Applicant's Name and Address: AGA Medical Corporation
682 Mendelssohn Avenue
Golden Valley, MN 55427
USA

Premarket Approval Application (PMA) Number: P020024

Date of Notice of Approval to Applicant: May 14, 2003

B. Indications And Usage

- The AMPLATZER Duct Occluder is a percutaneous, transcatheter occlusion device intended for the non-surgical closure of patent ductus arteriosus (PDA).

C. Contraindications

1. Patients weighing less than 6 kgs.
2. Patients less than 6 months of age.
3. Presence of thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained.
4. Active endocarditis or other infections producing bacteremia.
5. Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate the appropriate sheath size.
6. Patients with pulmonary hypertension with pulmonary vascular resistance of > 8 Woods units or Rp/Rs of > 0.4.

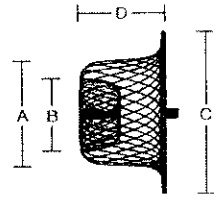
D. Warnings and Precautions

See warnings and precautions in the final labeling (Instructions for Use).

E. Device Description

The AMPLATZER Duct Occluder is a self-expandable device made from a Nitinol wire mesh. A retention skirt on the aortic side provides secure positioning in the ampulla of the ductus. As the occluder is implanted, it expands outward and the

wires push against the wall of the ductus. Polyester fabric is sewn into the occluder with polyester thread. The fabric induces thrombosis that closes the communication. The AMPLATZER Duct Occluder may be delivered using the 180° AMPLATZER® Delivery System. The AMPLATZER® 180° Exchange System is commercially approved for use with the AMLATZER Atrial Septal Occluder Device (P000039). The Exchange System may also be used with the Duct Occluder as a "bail out" delivery system that is identical to the AMPLATZER® 180° Delivery System with the exception of the dilator, which incorporates an enlarged inner lumen for passage over an AMPLATZER delivery cable.



A = Device Diameter at Descending Aorta
B = Device Diameter at Pulmonary Artery
C = Retention Skirt
D = Length

Figure 1 – AMPLATZER Duct Occluder

Table 1 - Device Specifications / Recommended sheath sizes

Order Number	A* Device Diameter at Descending Aorta	B* Device Diameter at Pulmonary Artery	C* Retention Skirt	D* Length	Recommended Sheath Size
9-PDA-003	5 mm	4 mm	9mm	5 mm	5-6 French, 180° Curve
9-PDA-004	6 mm	4 mm	10mm	7 mm	5-6 French, 180° Curve
9-PDA-005	8 mm	6 mm	12mm	7 mm	6 French, 180° Curve
9-PDA-006	10 mm	8 mm	16mm	8 mm	6-7 French, 180° Curve
9-PDA-007	12 mm	10 mm	18mm	8 mm	6-7 French, 180° Curve

*Refer to Figure 1.

The AMPLATZER 180° Delivery System includes:

- **Delivery Sheath** with Touhy-Borst Adapter - used to deliver the device. 180° indicates the curve of the sheath.
- **Dilator** – used to ease penetration of tissue.
- **Loading Device** – used to introduce the AMPLATZER Duct Occluder into the delivery sheath.
- **Plastic Vise** – facilitates directional control and serves as the "handle" for disconnecting (unscrewing) the delivery cable from the device.
- **Delivery Cable** – the device is screwed onto the distal tip of the delivery cable, which allows for placement (and if necessary, retrieval) of the device.

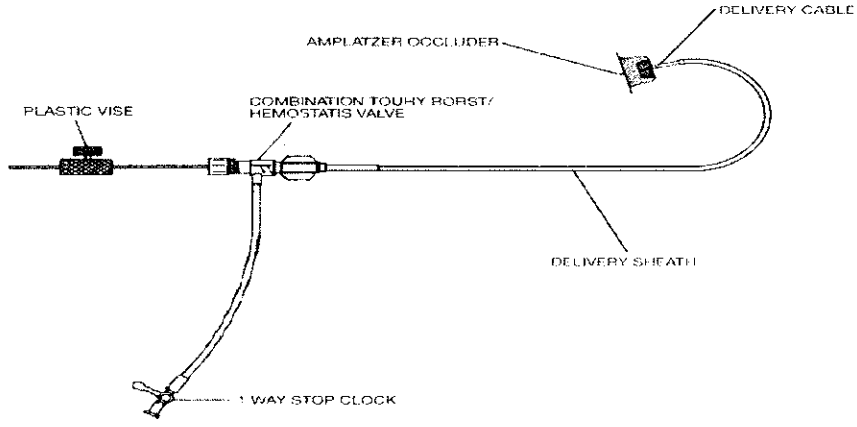


Figure 1 AMPLATZER Duct Occluder and Delivery System

The AMPLATZER 180° Exchange System components are identical to the AMPLATZER Delivery System, with the exception of the dilator, which incorporates an enlarged inner lumen for passage over an AMPLATZER delivery cable.

F. Alternative Practices or Procedures

- **Surgical Closure of PDA**
  Surgery involves the Patent Ductus Arteriosus to be tied off surgically through an incision in the chest.

- **Medical therapy**
  Medical therapy may be appropriate depending on the size of the duct, presence of calcification, age of the patient, and overall medical condition. If medical therapy is used, it causes the ductus/opening to narrow, causing decreased blood flow through it. With repeated medical therapy the opening will close.

- **No Treatment**

G. Marketing History

Commercial distribution of the AMPLATZER Duct Occluder device and AMPLATZER 180° Delivery System outside of the United States began in 1998 and this device is marketed in over 30 different countries including Argentina, New Zealand, Armenia, Oman, Australia, Pakistan, Belarus, Panama, Bulgaria, Peru, Canada, Poland, Chile, Qatar, China, Romania, Colombia, Russia, Costa Rica, Saudi Arabia, Cyprus, Singapore, Czech Republic, Slovak Republic, Egypt, Slovenia, EU Countries (CE mark), South Africa, Guatemala, Sri Lanka, Hong Kong, Taiwan, Hungary, Thailand, India, Tunisia, Israel, Turkey. Commercial distribution of the AMPLATZER 180° Exchange System began in 2001. The device, delivery and Exchange systems have not been withdrawn from any market for reasons related to safety and effectiveness.

H. Summary Of Preclinical Studies

1. Bench Testing

Bench testing was done to ensure that all initial design requirements were met and to demonstrate the strength and reliability of the device. Design verification of the device and its components has been conducted to verify that the device is safe for its intended use.

The following tests were conducted on the AMPLATZER Septal Occluder (ASO) (reference PMA P000039), or the AMPLATZER Duct Occluder (PDA), or both. Materials, manufacturing processes, and quality control are identical for the AMPLATZER Duct Occluder and the AMPLATZER Septal Occluder. The differences between the AMPLATZER Duct Occluder and the AMPLATZER Septal Occluder are (1) the shape of the occluders, and (2) the smaller AMPLATZER Duct Occluders are manufactured with smaller diameter wire.

ASO Device **PDA Device**

Figure 2

Product testing pertaining to and/or conducted on the AMPLATZER Duct Occluder is summarized below.

Table 2 - Summary of AMPLATZER Occluder Testing

Test	Samples		Specification	Results	
Pull Test Laser Weld – Marker Bands to Wire Braid	**Wire Dia.**	**N**	> 18 lbs.	**Wire Diameter**	**Mean ± SD (range) lbs**
	.003"	6		.003"	27.98 ± 3.69 (23.65 – 34.75)
	.004"	9		.004"	30.34 ± 2.56 (26.30 – 35.45)
Pull Test Laser Weld-Screw Attachment to Marker Bands	**Wire Dia.**	**N**	> 18 lbs.	**Wire Diameter**	**Mean ± SD (range) lbs**
	.003"	6		.003"	40.05 ± 6.41 (32.25 – 49.35)
	.004"	5		.004"	34.80 ± 7.57 (28.25 – 45.30)
Pull Test Delivery Cable screw and device end screw	5		> 18 lbs	**Mean ± SD (range) lbs** 26.37 ± 2.32 (23.35 – 29.15)	

Table 3 - Summary of AMPLATZER Delivery System and/or Exchange System Testing

Test	Samples		Specification	Results		
Delivery Sheath Kink Resistance	**Size**	**N**	The sheath must not kink during normal clinical use.	**Size**	**Mean ± SD (range) degrees**	
	5F	4		5F	87.5 ± 2.89 (85° - 90°)	
	6F	4		6F	113.75 ± 7.5 (105° - 120°)	
	7F	5		7F	131 ± 7.42 (120° - 140°)	
	8F	10		8F	105.5 ± 12.35 (90° - 130°)	
	9F	10		9F	118 ± 10.33 (105° - 135°)	
Delivery Cable - Kink Resistance	**Delivery Cable Dia.**	**N**	Delivery Cables will sustain a minimum deflection of 120° before the slightest misalignment (3-5) is noted in a static condition.	**Mean ± SD (range) degrees**		
	0.0435"	10		128.5 ± 8.18 (120° – 145°)		
	0.0745"	10		164.0 ± 10.21 (150° – 180°)		
Pull Tests - Delivery Sheath Hub to Tubing	**Size**	**N**	Pull strength must not be <3lbs.	**Size**	**Mean ± SD (range) lbs**	
	5F	4		5F	4.49 ± 0.58 (4.15 – 5.35)	
	6F	4		6F	9.41 ± 1.17 (8.2 – 11.0)	
	7F	5		7F	10.89 ± 1.14 (9.55 – 12.3)	
	8F	4		8F	11.36 ± 0.08 (11.3 – 11.45)	
	9F	4		9F	11.61 ± 0.13 (11.5 – 11.8)	
Pull Test – Delivery Cable – Cable to Cable Screw Weld Joint	N		12 pounds	**Mean ± SD (range) lbs**		
	10			46.1 ± 5.5 (37 - >50)		
Exterior Surface Condition – Exchange System Sheath and Dilator	Sheath/ Dilator size (2 separate lots tested)	N	Determine the exterior surface conditions of the external catheter shaft, free from extraneous matter, free from process and surface defects and should cause minimum trauma to vessels during use (ISO 10555.1, 4.3)	Pass/Fail (Sheath/Dilator)		
	6F 180° 6F 180°	13 13		Pass Pass		
Compression Force of Delivery Cable through Dilator (Exchange System)	Sheath size (2 separate lots tested)	N	Compression force required to pass the delivery cable through the exchange system dilator	Mean/SD/(lbs.)		
	6F 180° 6F 180°	13 13		0.235/0.038 0.227/0.044		
Hub Tests: Stress, Liquid, Aspiration (Exchange System)	Sheath or Dilator Size (Fr)		Quantity	Leak	Aspiration	Stress
	6F 180° Sheath 6F 180° Dilator		13 13	None Observed	None Observed	None Observed
	6F 180° Sheath 6F 180° Dilator		13 13	None Observed	None Observed	None Observed

2. MRI Compatibility

Two AMPLATZER Septal Occluders were placed in a water phantom, fixed with adhesive tape, and examined by a Siemens 1.5 Tesla MRI apparatus. Various imaging modalities were used and minimal artifacts were only observed in the object vicinity. The testing showed that the device is MRI compatible up to 1.5 Tesla. In addition, MRI testing was conducted in two patients (8 years old, 6 hours post-implant; 3 months old, 6 hours post-implant). In both cases, there was no evidence of device movement during the imaging.

3. Corrosion Testing

a) Corrosion – Bench Testing

The device was tested per ASTM F746. The Nitinol sample did not display the general pitting found on the 316 stainless steel sample. In addition, there was no indication of crevice corrosion on the nickel-titanium sample as was seen on the 316 stainless steel samples.

Eight devices were tested for corrosion potential. The devices were degreased, rinsed with deionized water and blown with dry air. The electrolyte was prepared by dissolving 36.9g reagent grade sodium chloride in deionized water. Following transfer to the corrosion cell, the electrolyte was deoxygenated by sparging with zero grade nitrogen for a minimum of 60 minutes.

The devices were suspended in the corrosion cell and maintained in the electrolyte at open circuit for 60 minutes before beginning the polarization scan (0.6 V/h). The electrochemistry was performed with a PAR 263 Potentiosatat.

In all devices the onset of corrosion occurred ca. 0.08 V from the open circuit potential. The corrosion potential (E_{CORR}) for the samples tested varied by ca. 0.08 V. The shape of the hysteresis curve indicates that localized corrosion may occur.

b) Corrosion – Animal Testing

Post mortem examination was conducted in an animal specimen wherein two devices were implanted (device #1 – implanted 18 months and device #2 implanted 14 months). Although the animal was implanted with the AMPLATZER Muscular Ventricular Septal Occluder device, materials and methods are identical to the AMPLATZER Duct Occluder.

Analysis revealed both devices were nearly covered by neoendocardium. Gross inspection revealed no wire breakage. Light microscopy at 40x revealed a smooth surface. Scanning electron microscopy was carried out and compared to a new control wire. Both surfaces appeared identical. The wire surface appearance was typical of oxidized Nitinol wire.

Both devices were weighed (275 mg and 156 mg). No evidence of corrosion was observed for either device.

c) **Abrasion**

A device was explanted from a swine after 3 months (at least 26 million cycles). A biopsy was taken from the neo-endocardium for histologic examination. The device was examined grossly, by light microscopy and by scanning electron microscopy (SEM). No broken wires were detected.

SEM examinations were made at randomly selected wire intersection on both the large and small discs. The typical condition of the wires at the intersections were photographed. Results indicate that there are no signs of intersecting wires abrading each other.

4. **Biocompatibility Tests**

The AMPLATZER Duct Occluder is constructed of Nitinol (a nickel-titanium alloy) and polyester. The materials and manufacturing methods used to construct the AMPLATZER Duct Occluder are identical to those used to construct the approved AMPLATZER ASO device (P000039).

5. **Useful Life (Sterilization/Shelf Life)**

The AMPLATZER Duct Occluder, 180° Delivery System and 180° Exchange System are single-use devices which are provided sterile (via ethylene oxide) to the user. The sterilization cycle was validated to ensure successful sterilization to a Sterility Assurance Level (SAL) of 10^{-6}.

Product and package stability testing of the AMPLATZER Duct Occluder, 180° Delivery System, and 180° Exchange System was performed. Visual inspection and physical testing indicated that the device performed within product specification for up to 3 years. Based upon these results, an expiration date of 3 years has been established.

6. **Animal Testing**

Animal studies were conducted to evaluate the device design and to demonstrate that the AMPLATZER Duct Occluder was capable of providing rapid closure and endothelialization of patent ductus arteriosus defects without evidence of residual shunting. Percutaneous closure of surgically placed aortopulmonary conduits was attempted in 19 dogs. The occluder consisted of 13 nonfilled frames and 6 polyester filled frames. Results obtained indicated shunt closure occurred in seven of 17 animals (41%) at 30 minutes, in 12 of 17 animals (71%) at 1 week, in 14 of 17 animals (82%) at 3 months. Significantly higher 30-minute closure rates were noted with polyester augmented occluders compared with nonfilled occluders (five of five [100%] vs. two of 12 [17%]; P = .002). Persistent shunt at 3 months occurred in only one nonfilled device (6%). In the remaining 16 cases, both shunt orifices were completely or nearly completely covered by neoendothelium.

I. *Adverse Events*

The AMPLATZER Duct Occluder was evaluated in a multi-center, non-randomized, pivotal study evaluating the clinical performance for PDA closure. 435 patients received 435 devices with a total device exposure of 371.9 years. Individual patient exposure to the device averaged 10.4 months (ranging from 0.0 – 28.5 months).

There was one death reported five months post-procedure. The Data Safety Monitoring Board members reviewed this adverse event and were unable to determine if the death was device related.

Table 5-Adverse Events Summary

Adverse Event Definition[1,2]	**Number of Patients**	**95% Upper Confidence Bound**
Serious Adverse Event		
Death	1/393 (0.3%)	
Major Adverse events		
Device Embolization with percutaneous removal	1/393 (0.3%)	
Thrombus on Device	1/393 (0.3%)	
Partial Obstruction of Pulmonary Artery	1/393 (0.3%)	
Pseudo aneurysm	1/393 (0.3%)	
Total Serious and Major Adverse Events	5/393 (1.2%)	2.7%
Minor Adverse Events		
Hematoma of the groin	7/393 (1.7%)	
Other[3]	6/393 (1.5%)	
Loss of peripheral pulse	4/393 (1.0%)	
Cardiac arrhythmia requiring cardioversion or medication	2/393 (0.5%)	
Any Adverse Event	23/393 (5.9%)	8.2%

[1]One patient had a Major and Minor Adverse event. 23 patients had 24 adverse events.
[2]Patients less than 6 months of age, and less than 6 kg are not included in this analysis.
[3]Air embolism, allergic reaction, blood loss/no transfusion, laryngospasm, respiratory arrest, thrombus on device

Definitions:

Death – death during or after the procedure due to complications of the procedure.
Device embolization – embolization with transcatheter removal.
Thrombus – thrombus on device with or without embolization.
Partial Obstruction of Pulmonary Artery – increase in the pressure gradient of > 10mmHg and a lung perfusion scan with >30% flow to the LPA.
Pseudoaneurysm – false aneurysm of the femoral hematoma requiring treatment.
Loss of peripheral pulse – transient or requiring only heparin therapy.
Cardiac arrhythmia – requiring cardioversion or medication.

Potential Adverse Events

Placement of the AMPLATZER Duct Occluder involves using standard interventional cardiac catheterization techniques. In addition to the above observed adverse events, the following are potential adverse events listed in alphabetical order that were not observed in the clinical study. The following events might occur from either the catheterization procedure or from the device:

- Air Embolus
- Allergic dye reaction
- Allergic drug reaction
- Anesthesia reactions
- Apnea
- Arrhythmia
- Bacterial endocarditis
- Bleeding
- Brachial plexus injury
- Chest pain
- Delivery system failure
- Fever
- Headache/Migraine
- Hyper/Hypotension
- MI
- Perforation of vessel or myocardium
- Peripheral Embolism
- Stroke/TIA
- Thrombus
- Valvular regurgitation
- Vascular access site complications

J. Summary Of Clinical Studies

Purpose: The purpose of the trial was to evaluate the safety and effectiveness of the AMPLATZER Duct Occluder for the non-surgical closure of patent ductus arteriosus (PDA).

Conclusions: In selected patients, use of the AMPLATZER Duct Occluder demonstrated effective defect closure and acceptable rates of adverse events when compared to Objective Performance Criteria (OPC).

Design: The AMPLATZER Duct Occluder was evaluated in a multi-center, non-randomized, pivotal study evaluating the clinical performance for PDA closure. The OPC formulated the following specific outcome measure criteria as guidelines for safety and efficacy of the AMPLATZER Duct Occluder: the Primary Efficacy Outcome measure (complete closure) greater than 85% at 12 months, the clinical examination closure (absence of continuous heart murmur) greater than 95% at 12 months, and the Serious and Major adverse event rate less than 6%.

Attempt to treat was initiated in 441 patients. Enrolled patients had angiographic or echocardiographic evidence of patent ductus arteriosus and body weight $\geq$ 5 Kilograms. Exclusion criteria included:

- Pulmonary vascular resistance above 8 Woods units or a Rp/Rs>0.4.
- Additional cardiac or non-cardiac abnormalities that could reasonably be expected to significantly affect the patient's health adversely in the next two years, i.e.; cancer, Eisenmenger's syndrome, other serious congenital heart disease.
- Pelvic vein or inferior vena cava thrombosis.

- Sepsis (local/generalized) or any type of infection that could not be successfully treated prior to device placement.
- History of repeated pulmonary infection
- Demonstrated intracardiac thrombi on echocardiography.
- Inability to obtain informed consent.

A total of 441 patients were enrolled in the clinical study. Of the 441 patients, 6 patients were acute procedure failures and did not receive the device, 42 patients were less than 6 kgs. in weight or were younger than 6 months of age. Thus 393 patients were evaluated for effectiveness and safety in the following tables.

Demographics: Factors evaluated included age (mean 7.2 +/- 12.2 years; range 0.5-70.7) gender (68% female; 32% male) and weight (mean 21.9 +/- 22.3 kilograms; range 6.1, 164.5) and presence of continuous murmur (94.4%).

Methods: Patients with clinical symptoms of patent ductus arteriosus who were being evaluated for PDA closure underwent physical examination, an electrocardiogram, a chest x-ray, and an echocardiogram to assess the presence of ductus and to assess left pulmonary artery stenosis.

Device placement was attempted in 441 patients. The patients underwent baseline evaluations and pre-closure angiographic measurements. 435 patients received devices. No patient had two devices implanted.

The patients were instructed to avoid strenuous activity for a period of one month. Endocarditis prophylaxis was carried out for 6 months according to the recommendation of the American Heart Association. Additionally, patients were examined and a Transthoracic Echocardiogram (TTE) was conducted at 24 hours, 6 months and 1 year.

Results: A total of 390/393 (99.2%) of patients were successfully implanted with the AMPLATZER Duct Occluder. There were 5/393 (1.3%) patients with serious and major adverse events reported, and 19/393 (4.8%) patients experienced a minor adverse event. Overall, 23/393 (5.8%) of enrolled patients experienced an adverse event. Complete closure of the ductus was 98.4% at the 6-month interval and 98.6% at the 12-month interval. The composite success rate at 12-months was 96.7%. Please refer to Table 6 for all Principal Safety and Efficacy Results.

Table 6 - Principal Safety and Efficacy Results

Principal Efficacy	Patient	Percent	95% Lower Confidence Bound
Acute Procedure Success	390/393	99.2%	98.0%
Acute Efficacy	308/393	78.4%	74.7%
Pre Discharge Efficacy	354/392	90.3%	87.5%
6 Month Efficacy	312/317	98.4%	96.7%
12 Month Efficacy	205/208	98.6%	96.3%
Heart Murmur Success	201/201	100.0%	98.5%
Composite Success	205/212	96.7%	93.9%
Extended Efficacy	265/268	98.9%	97.1%
Carry Forward Efficacy	383/390	98.2%	96.7%
Principal Safety (Adverse Events)[1,2,3]			
Serious	1 / 393	0.3%	1.2%
Major	4 / 393	1.0%	
Total Serious and Major	5 / 393	1.3%	2.7%
Minor	19 / 393	4.8%	
Any Adverse Event	23 / 393	5.9%	8.2%

[1] One patient had a Major and Minor Adverse event. 23 patients had 24 adverse events.
[2] Definitions for Adverse events can be found in Table 2.
[3] Patients less than 6 months of age, and less than 6 kgs. are not included in this analysis.

Acute Procedure Success - Of the number of patients where the device was attempted, those who successfully received a device.
Acute Efficacy – Of the number of patients where the device was attempted, those who had complete closure of the ductus at procedure.
Pre-Discharge Efficacy - Complete closure of the ductus at pre-discharge in the attempted patients.
6 Month Efficacy - Complete closure of the ductus at the 6 month visit in the attempted patients.
12-month Efficacy - Complete closure of the ductus as measured by echocardiography at the 12 month visit.
Heart Murmur Success – Clinical closure of the PDA as measured by absence of continuous heart murmur at the 12 month visit.
Composite Success - Device attempt with successful placement without a serious or major adverse event, surgical reintervention, embolization, or residual shunt at the 12-month visit.
Extended Efficacy – Complete closure of the ductus at the 12 month or longer visit in the attempted patients.
Carry Forward Efficacy – Complete closure of the ductus at the last visit.

K. Device Failures and Replacements

Device: Reported device failures include difficulty screwing the device to the delivery cable.

Delivery System: Reported delivery system failures are shown in the following table.

Complaint	Rate N (%)
Sheath/dilator (including kink, dilator/sheath compatibility, inability to load the device)	29 (59%)
Delivery Cable (including loose wire, screw problems, unable to remove pin vise)	18 (37%)
Hemostasis Valve Assembly	2 (4%)

A field correction was issued in November, 2002, because of a potential problem with the AMPLATZER Delivery and Exchange Systems. The analysis of returned product revealed that some devices included a delivery cable end screw that was undersized and/or the female end screw attachment on the device was of poor quality (i.e., incomplete threads). In order to address these issues, alternative suppliers for the screw components were qualified and additional inspection procedures were instituted. Note that these reported malfunctions do not appear to be associated with adverse clinical outcomes

L. Conclusions Drawn From The Studies

Effectiveness of the AMPLATZER Duct Occluder has been demonstrated by successful closure of PDA at the 12-month follow-up. Complete closure by echocardiography was 98.6%. The total serious and major adverse event rate associated with the AMPLATZER Duct Occluder of 1.3% demonstrates the device provides a reasonable assurance of safety in the closure of PDA in the intended population.

In conclusion, the AMPLATZER® Duct Occluder operates as designed and provides a reasonable assurance of safety and effectiveness in the intended patient population.

M. Panel Recommendation

This application was not the subject of full review by the Circulatory System Devices Panel; however, a homework assignment was issued to two current members. In consideration of Panel member input, the device labeling was modified to include contraindications for patients < 6kg and/or < 6 years of age and a warning for patients over 40 years of age. In addition, a 5-year post-approval study was included as a condition of approval in order to monitor any changes associated with patient growth and increased implant time.

N. CDRH Decision

CDRH conveyed the Conditions of Approval including the Post-Approval Study Requirement to AGA Medical in a facsimile dated April 10, 2002. AGA Medical indicated concurrence with those Conditions of Approval.

The applicant's manufacturing facility was inspected on June 12 and December 6, 2002 and contract sterilization facility was inspected on May 1, 2001. These facilities were found to be in compliance with the device Quality System Regulation (Part 820).

FDA issued an approval order on May 14, 2003.

O. Approval Specifications

Directions for Use: See labeling.

Hazards to Health from Use of the Device: See INDICATIONS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE EVENTS in the labeling.

Post-approval Requirements and Restrictions: See Approval Order